

Applicants: Reiter, et al
U.S. Serial No. 09/359,326
Filed: July 20, 1999
Page: 2

Please amend the subject application as follows:

IN THE TITLE:

Please replace the title paragraph beginning at page 1, line 1 with the following rewritten title:
-- ANTIBODIES TO PROSTATE STEM CELL ANTIGEN PROTEIN --.

IN THE SPECIFICATION :

Please replace the paragraph beginning at page 1, line 3 with the following rewritten paragraph:

C1
-- This application is a continuation-in-part (CIP) of U.S. Serial No. 09/308,503, filed May 25, 1999, which is a CIP of U.S. Serial No. 09/251,835, filed February 17, 1999, which is a continuation-in-part (CIP) of U.S. Serial No. 09/203,939, filed December 2, 1998, which is a CIP of U.S. Serial No. 09/038,261, filed March 10, 1998; claiming the priority of provisional applications, U.S. Serial No. 60/228,816, filed March 10, 1997; U. S. Serial No. 60/071,141 filed January 12, 1998 and; U. S. Serial No. 60/ 074,675, filed February 13, 1998. This application further claims the benefit of the filing dates of U.S. Serial Nos. 60/124,658 filed March 16, 1999; 60/120,536 filed February 17, 1999; and 60/113,230 filed December 21, 1998. The contents of all of the foregoing applications are incorporated by reference into the present application. -- .

Please replace the paragraph beginning at page 6, line 3 with the following rewritten paragraphs:

C2
-- FIG. 1A. Nucleotide sequence (SEQ ID NO:1, ATCC Designation 209612) of a cDNA encoding human PSCA.

FIG. 1B. Translated amino acid sequence (SEQ ID NO:2) of human PSCA. -- .

Please replace the paragraph beginning at page 6, line 6 with the following rewritten paragraph:

C³ **FIG. 2.** Nucleotide sequence (SEQ ID NO:3), of a murine cDNA PSCA homologue and the translated amino acid sequence (SEQ ID NO:4) of murine PSCA.--

Please replace the paragraph beginning at page 6, line 8 with the following rewritten paragraph:

C⁴ **FIG. 3.** Alignment of amino acid sequences of human PSCA (SEQ ID NO:5), murine PSCA (SEQ ID NO:6), and human stem cell antigen-2 (hSCA-2) (SEQ ID NO:7). Shaded regions highlight conserved amino acids. Conserved cysteines are indicated by bold lettering. Four predicted N-glycosylation sites in PSCA are indicated by asterisks. The underlined amino acids at the beginning and end of the protein represent N terminal hydrophobic signal sequences and C terminal GPI-anchoring sequences, respectively.--

Please replace the paragraph beginning at page 6, line 21 with the following rewritten paragraphs:

C⁵ **FIG. 7A.** Restricted Expression of PSCA mRNA in normal and cancerous tissues. RT-PCR analysis of PSCA expression in normal human tissues demonstrating high expression in prostate, placenta, and tonsils. 1ng of reverse-transcribed first strand cDNA (Clontech, Palo Alto, CA) from the indicated tissues was amplified with PSCA gene specific primers. Data shown are from 30 cycles of amplification.

FIG. 7B. Restricted Expression of PSCA mRNA in normal and cancerous tissues. RT-PCR analysis of PSCA expression demonstrating high level in prostate cancer xenografts and normal tissue. 5 ng of reverse-transcribed cDNA from the indicated tissues was amplified with PSCA gene specific primers. Amplification with β -actin gene specific primers demonstrate normalization of the first strand cDNA of the various samples. Data shown are from 25 cycles of amplification. AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line.--

Please replace the paragraph beginning at page 7, line 1 with the following rewritten paragraphs:

C6 **FIG. 8A.** Schematic representation of human Thy-1/Ly-6 gene structures.

FIG. 8B. Schematic representation of murine PSCA gene structure.

FIG. 8C. Schematic representation of human PSCA gene structure.

Please replace the paragraph beginning at page 7, line 5 with the following rewritten paragraphs:

C7 **FIG. 9A.** Northern blot analysis of PSCA expression. Total RNA from normal prostate and LAPC-4 androgen dependent (AD) and independent (AI) prostate cancer xenografts were analyzed using PSCA or PSA specific probes. Equivalent RNA loading and RNA integrity were demonstrated separately by ethidium staining for 18S and 28S RNA.

FIG. 9B. Northern blot analysis of PSCA expression. Human multiple tissue Northern blot analysis of PSCA. The filter was obtained from Clontech (Palo Alto, CA) and contains 2ug of polyA RNA in each lane.

Please replace the paragraph beginning at page 7, line 12 with the following rewritten paragraphs:

C8 **FIG. 10A.** Northern blot analysis of PSCA expression in prostate cancer xenografts and tumor cell lines. PSCA demonstrates high level prostate cancer specific gene expression. 10 µg of total RNA from the indicated tissues were size fractionated on an agarose/formaldehyde gel, transferred to nitrocellulose, and hybridized sequentially with ³²P-labelled probes representing PSCA cDNA fragments. Shown are 4 hour and 72 hour autoradiographic exposures of the membrane. BPH, benign prostatic hyperplasia; AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line.

FIG. 10B. Northern blot analysis of PSM expression in prostate cancer xenografts and tumor cell lines. PSM demonstrates high level prostate cancer specific gene expression. 10 µg of total RNA from the indicated tissues were size fractionated on an agarose/formaldehyde gel, transferred to nitrocellulose, and hybridized sequentially with ³²P-labelled probes representing PSM cDNA fragments. Shown are 4 hour and 72 hour autoradiographic exposures of the membrane. BPH, benign prostatic hyperplasia; AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line.

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FIG. 10C. Northern blot analysis of PSA expression in prostate cancer xenografts and tumor cell lines. 10 µg of total RNA from the indicated tissues were size fractionated on an agarose/formaldehyde gel, transferred to nitrocellulose, and hybridized sequentially with ³²P-labelled probes representing PSA cDNA fragments. Shown are 4 hour and 72 hour autoradiographic exposures of the membrane and the ethidium bromide gel demonstrating equivalent loading of samples. BPH, benign prostatic hyperplasia; AD, androgen-dependent; AI, androgen-independent; IT, intratibial xenograft; C.L., cell line.

Please replace the paragraph beginning at page 7, line 21 with the following rewritten paragraphs:

C9
--**FIG. 11A.** In situ hybridization with antisense riboprobe for human PSCA on normal prostate specimens. PSCA is expressed by a subset of basal cells within the basal cell epithelium (black arrows), but not by the terminally differentiated secretory cells lining the prostatic ducts (400X magnification).

FIG. 11B. In situ hybridization with antisense riboprobe for human PSCA on normal and malignant prostate specimens. PSCA is expressed strongly by a high grade prostatic intraepithelial neoplasia (PIN) (black arrow) and by invasive prostate cancer glands (yellow arrows), but is not detectable in normal epithelium (green arrow) at 40X magnification.

C⁹
int **FIG. 11C.** In situ hybridization with antisense riboprobe for human PSCA on malignant prostate specimens. Strong expression of PSCA in a case of high grade carcinoma (200X magnification).

Please replace the paragraph beginning at page 7, line 29 (and continuing through page 8, line 7) with the following rewritten paragraphs:

--**FIG. 12A.** Biochemical analysis of PSCA. PSCA was immunoprecipitated from 293T cells transiently transfected with a PSCA construct and then digested with either N-glycosidase F or O-glycosidase, as described in Materials and Methods.

FIG. 12B. Biochemical analysis of PSCA. PSCA was immunoprecipitated from 293T transfected cells, as well as from conditioned media of these cells. Cell-associated PSCA migrates higher than secreted or shed PSCA on a 15% polyacrylamide gel.

C¹⁰ **FIG 12C.** Biochemical analysis of PSCA. FACS analysis of mock-transfected 293T cells, PSCA-transfected 293T cells, and LAPC-4 prostate cancer xenograft cells using an affinity purified polyclonal anti-PSCA antibody. Cells were not permeabilized in order to detect only surface expression. The y axis represents relative cell number and the x axis represents fluorescent staining intensity on a logarithmic scale. --

Please replace the paragraph beginning at page 8, line 17 with the following rewritten paragraphs:

--**FIG. 14A.** Flow Cytometric analysis of cell surface PSCA expression on prostate cancer xenograft (LAPC-9) using anti-PSCA monoclonal antibodies 1G8 and 3E6, mouse anti-PSCA polyclonal serum, or control secondary antibody. See Example 5 for details.

C¹¹ **FIG. 14B.** Flow Cytometric analysis of cell surface PSCA expression on prostate cancer cell line (LAPC-4) using anti-PSCA monoclonal antibodies 1G8 and 3E6, mouse anti-PSCA polyclonal serum, or control secondary antibody. See Example 5 for details.

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C12
FIG 14C. Flow Cytometric analysis of cell surface PSCA expression on normal prostate epithelial cells (PreC) using anti-PSCA monoclonal antibodies 1G8 and 3E6, mouse anti-PSCA polyclonal serum, or control secondary antibody. See Example 5 for details. -- .

Please replace the paragraph beginning at page 8, line 22 with the following rewritten paragraphs:

-- **FIG. 15A.** An epitope map for each of the seven disclosed antibodies.

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FIG 15B. Epitope mapping of anti-PSCA monoclonal antibodies conducted by Western blot analysis of GST-PSCA fusion proteins. -- .

Please replace the paragraph beginning at page 8, line 26 with the following rewritten paragraphs:

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-- **FIG. 16A.** Alignment of amino acid sequences of human PSCA, murine PSCA, and human stem cell antigen-2 (hSCA-2). Shaded regions highlight conserved amino acids.

FIG. 16B A schematic diagram showing that PSCA is a GPI-anchored protein. -- .

Please replace the paragraph beginning at page 11, line 19 with the following rewritten paragraph:

C14
-- **FIG. 37.** A photograph showing immunological reactivity of anti-mAbs. Immunoprecipitation of PSCA from 293T cells transiently transfected with PSCA using mAbs 1G8, 2H9, 3C5, 3E6 and 4A10. The control was an irrelevant murine IgG mAb. -- .

Please replace the paragraph beginning at page 12, line 4 with the following rewritten paragraphs:

C15-
-- **FIG. 39A.** Expression of PSCA in normal tissues. Panel *a* shows staining of bladder transitional epithelium with mAb 1G8. Panel *b* shows colonic neuroendocrine cell staining with mAb 1G8. Double staining with chromogranin confirmed that the positive cells are of neuroendocrine origin (not shown). Panel *c* shows staining of collecting ducts (arrow) and tubules with mAb 3E6. Panel *d* show staining of placental trophoblasts with mAb 3E6.

FIG. 39B. Expression of PSCA in normal tissues. Northern blot analysis of PSCA mRNA expression. Total RNA from normal prostate, kidney, bladder and the LAPC-9 prostate cancer xenograft was analyzed using a PSCA specific probe (top panel). The same membrane was probed with actin to control of loading differences (bottom panel). -- .

Please replace the paragraph beginning at page 12, line 13 with the following rewritten paragraphs:

-- **FIG. 40A.** Targeting of mouse PSCA gene. A schematic drawing showing a strategy for creating a PSCA targeting vector.

C16
FIG. 40B. Targeting of mouse PSCA gene. A photograph of a Southern blot analysis of genomic DNA using 3' probe showing recovery of wild-type (+/+) and heterozygous (+/-) ES cells. -- .

Please replace the paragraph beginning at page 13, line 7 with the following rewritten paragraphs:

C17
~~#~~**FIG. 47A.** Photograph of a multiple tissue Northern blot analysis showing tissue specific expression patterns of human PSCA RNA.

FIG. 47B. Photograph of a multiple tissue Northern blot analysis showing tissue specific expression patterns of murine PSCA RNA. ψ .

Please replace the paragraph beginning at page 15, line 21 with the following rewritten paragraph:

C18 **FIG. 58.** Nucleotide sequence (SEQ ID NO:10) and amino acid sequence (SEQ ID NO:11) of the heavy chain variable domain regions of PSCA monoclonal antibodies 1G8. CDRs are labeled and underlined. *tu*.

Please replace the paragraph beginning at page 15, line 24 with the following rewritten paragraph:

C19 **FIG. 59.** Nucleotide sequence (SEQ ID NO:12) and amino acid sequence (SEQ ID NO:13) of the heavy chain variable domain regions of PSCA monoclonal antibodies 4A10. CDRs are labeled and underlined. *tu*.

Please replace the paragraph beginning at page 15, line 27 with the following rewritten paragraph:

C20 **FIG. 60.** Nucleotide sequence (SEQ ID NO:14) and amino acid sequence (SEQ ID NO:15) of the heavy chain variable domain regions of PSCA monoclonal antibodies 2H9. CDRs are labeled and underlined. *tu*.

Please replace the paragraph beginning at page 18, line 1 with the following rewritten paragraph:

C21 **One aspect of the invention provides various PSCA proteins and peptide fragments thereof. As used herein, PSCA refers to a protein that has the amino acid sequence of human PSCA (SEQ ID NO:2) as provided in FIGS. 1B and 3, the amino acid sequence of the murine PSCA homologue (SEQ ID NO:4) as provided in FIG. 3, or the amino acid sequence of other mammalian PSCA homologues, as well as allelic variants and conservative substitution mutants of these proteins that have PSCA activity. The PSCA proteins of the invention include the specifically identified and characterized variants herein described, as well as allelic variants, conservative substitution variants and homologs that can be isolated/generated and characterized without undue experimentation following the methods outlined below. For the sake of convenience, all PSCA proteins will be collectively referred to as the PSCA proteins, the proteins of the invention, or PSCA.**

Please replace the paragraph beginning at page 18, line 12 with the following rewritten paragraph:

C22 --] The term "PSCA" includes all naturally occurring allelic variants, isoforms, and precursors of human PSCA (SEQ ID NO:2) as provided in FIGS. 1B and 3 and murine PSCA (SEQ ID NO:4) as provided in FIG. 3. In general, for example, naturally occurring allelic variants of human PSCA will share significant homology (e.g., 70 - 90%) to the PSCA amino acid sequence provided in FIGS. 1B and 3. Allelic variants, though possessing a slightly different amino acid sequence, may be expressed on the surface of prostate cells as a GPI linked protein or may be secreted or shed. Typically, allelic variants of the PSCA protein will contain conservative amino acid substitutions from the PSCA sequence herein described or will contain a substitution of an amino acid from a corresponding position in a PSCA homologue such as, for example, the murine PSCA homologue described herein. -- .

Please replace the paragraph beginning at page 18, line 22 with the following rewritten paragraph:

C23 --] One class of PSCA allelic variants will be proteins that share a high degree of homology with at least a small region of the PSCA amino acid sequences presented in FIGS. 1B (SEQ ID NO:2) and 3 (SEQ ID NO: 2 or 4), but will further contain a radical departure from the sequence, such as a non-conservative substitution, truncation, insertion or frame shift. Such alleles are termed mutant alleles of PSCA and represent proteins that typically do not perform the same biological functions.

Please replace the paragraph beginning at page 19, line 12 with the following rewritten paragraph:

C24 ~~4~~ The amino acid sequence of human PSCA protein (SEQ ID NO:2) is provided in FIGS. 1B and 3. Human PSCA is comprised of a single subunit of 123 amino acids and contains an amino-terminal signal sequence, a carboxy-terminal GPI-anchoring sequence, and multiple N-glycosylation sites. PSCA shows 30% homology to stem cell antigen-2 (SCA-2), a member of the Thy-1/Ly-6 gene family, a group of cell surface proteins which mark the earliest phases of hematopoietic development. The amino acid sequence of a murine PSCA homologue (SEQ ID NO:4) is shown in FIG. 3. Murine PSCA is a single subunit protein of 123 amino acids having approximately 70% homology to human PSCA and similar structural organization. ~~7~~.

Please replace the paragraph beginning at page 19, line 21 with the following rewritten paragraph:

C25 -- PSCA proteins may be embodied in many forms, preferably in isolated form. As used herein, a protein is said to be isolated when physical, mechanical or chemical methods are employed to remove the PSCA protein from cellular constituents that are normally associated with the protein. A skilled artisan can readily employ standard purification methods to obtain an isolated PSCA protein. A purified PSCA protein molecule will be substantially free of other proteins or molecules that impair the binding of PSCA to antibody or other ligand. The nature and degree of isolation and purification will depend on the intended use. Embodiments of the PSCA protein include a purified PSCA protein and a functional, soluble PSCA protein. One example of a functional soluble PSCA protein has the amino acid sequence shown in FIG. 1B (SEQ ID NO:2) or a fragment thereof. In one form, such functional, soluble PSCA proteins or fragments thereof retain the ability to bind antibody or other ligand. -- .

Please replace the paragraph beginning at page 20, line 4 with the following rewritten paragraph:

C26 --The invention also provides peptides comprising biologically active fragments of the human (SEQ ID NO:2) and murine (SEQ ID NO:4) PSCA amino acid sequences shown in FIGS. 1B and 3. For example, the invention provides a peptide fragment having the amino acid sequence TARIRAVGLLTVISK (SEQ ID NO:16), a peptide fragment having the amino acid sequence VDDSQDYYVGKK (SEQ ID NO:17), and SLNCVDDSQDYYVGK (SEQ ID NO:18). -- .

Please replace the paragraph beginning at page 24, line 15 with the following rewritten paragraph:

C27 ¶ Various methods for the preparation of antibodies are well known in the art. For example, antibodies may be prepared by immunizing a suitable mammalian host using a PSCA protein, peptide, or fragment, in isolated or immunoconjugated form (Harlow, Antibodies, Cold Spring Harbor Press, NY (1989)). In addition, fusion proteins of PSCA may also be used, such as a PSCA GST-fusion protein. Cells expressing or overexpressing PSCA may also be used for immunizations. Similarly, any cell engineered to express PSCA may be used. This strategy may result in the production of monoclonal antibodies with enhanced capacities for recognizing endogenous PSCA. For example, using standard technologies described in Example 5 and standard hybridoma protocols (Harlow and Lane, 1988, Antibodies: A Laboratory Manual. (Cold Spring Harbor Press)), hybridomas producing monoclonal antibodies designated 1G8 (ATCC No. HB-12612), 2A2 (ATCC No. HB-12613), 2H9 (ATCC No. HB-12614), 3C5 (ATCC No. HB-12616), 3E6 (ATCC No. HB-12618), and 3G3 (ATCC No. HB-12615), 4A10 (ATCC No. HB-12617) were generated. These antibody were deposited on December 11, 1998 with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209. ¶ .

Please replace the paragraph beginning at page 32, line 21 with the following rewritten paragraph.

C 28
-- The nucleotide sequence of a cDNA (SEQ ID NO:1) encoding one allelic form of human PSCA is provided in FIG. 1A. The nucleotide sequence of a cDNA (SEQ ID NO:3) encoding a murine PSCA homologue ("murine PSCA") is provided in FIG. 2. Genomic clones of human and murine PSCA have also been isolated, as described in Example 4. Both the human and murine genomic clones contain three exons encoding the translated and 3' untranslated regions of the PSCA gene. A fourth exon encoding a 5' untranslated region is presumed to exist based on PSCA's homology to other members of the Ly-6 and Thy-1 gene families (**FIG. 8**). -- .

Please replace the paragraph beginning at page 39, line 20 with the following rewritten paragraph.

C 29
-- First, a nucleic acid molecule is obtained that encodes a PSCA protein (SEQ ID NO: 2 or 4) or a fragment thereof, such as the nucleic acid molecule depicted in FIG. 1A. The PSCA-encoding nucleic acid molecule is then preferably placed in an operable linkage with suitable control sequences, as described above, to generate an expression unit containing the PSCA-encoding sequence. The expression unit is used to transform a suitable host and the transformed host is cultured under conditions that allow the production of the PSCA protein. Optionally the PSCA protein is isolated from the medium or from the cells; recovery and purification of the protein may not be necessary in some instances where some impurities may be tolerated. -- .

Please replace the paragraph beginning at page 74, line 5 with the following rewritten paragraph.

C 30
4 Sequence analysis revealed that clone #15 had no exact match in the databases, but shared 30% nucleotide homology with stem cell antigen 2, a member of the Thy-1/Ly-6 superfamily of glycosylphosphatidylinositol (GPI)-anchored cell surface antigens. Clone #15 encodes a 123 amino acid protein (SEQ ID NO:2) which is 30% identical to SCA-2 (SEQ ID NO:5) (also called RIG-E) and contains a number of highly conserved cysteine residues characteristic of the Ly-6/Thy-1 gene family (FIG. 3). Consistent with its homology to a family of GPI-anchored proteins, clone #15 contains both an amino-terminal hydrophobic signal sequence and a carboxyl-terminal stretch of hydrophobic amino acids preceded by a group of small amino acids

C30
W/ defining a cleavage/binding site for GPI linkage (Udenfriend and Kodukula, 1995, Ann. Rev. Biochem. 64: 563-591). It also contains four predicted N-glycosylation sites. Because of its strong homology to the stem cell antigen-2, clone #15 was renamed prostate stem cell antigen (PSCA). 5' and 3' PCR RACE analysis was then performed using cDNA obtained from the LAPC-4 androgen independent xenograft and the full length cDNA nucleotide sequence (including the coding and untranslated regions) was obtained. The nucleotide sequence of the full length cDNA (SEQ ID NO:1) encoding human PSCA is shown in FIG. 1A and the translated amino acid sequence (SEQ ID NO:2) is shown in FIG. 1B and in FIG. 3. -- .

Please replace the paragraph beginning at page 79, line 17 with the following rewritten paragraph.

C31
The human PSCA cDNA was used to search murine EST databases in order to identify homologues for potential transgenic and knockout experiments. One EST obtained from fetal mouse and another from neonatal kidney were 70% identical to the human cDNA at both the nucleotide and amino acid levels. The homology between the mouse clones and human PSCA included regions of divergence between human PSCA and its GPI-anchored homologues, indicating that these clones likely represented the mouse homologue of PSCA. Alignment of these ESTs and 5' extension using RACE-PCR provided the entire coding sequence (SEQ ID NO:4) (FIG. 2). #.

Please replace the paragraph beginning at page 81, line 12 with the following rewritten paragraph.

-- **Generation and Production of Monoclonal Antibodies.** BALB/c mice were immunized three times with a purified PSCA-glutathione S-transferase (GST) fusion protein containing PSCA amino acids 22-99 (SEQ ID NO:2) (FIG. 1B). Briefly, the PSCA coding sequence corresponding to amino acids 18 through 98 of the human PSCA amino acid sequence was PCR-amplified using the primer pair:

C32 5'- GGAGAATTCATGGCACTGCCCTGCTGTGCTAC
3'-GGAGAATTCCTAATGGGCCCCGCTGGCGTT

The amplified PSCA sequence was cloned into pGEX-2T (Pharmacia), used to transform E. coli, and the fusion protein isolated.

Please replace the paragraph beginning at page 97, line 6 with the following rewritten paragraph.

C33 * Directly labeled fluorescent DNA probes for PSCA and for the 8q24 (c-myc) region were chosen. The PSCA cDNA (SEQ ID NO:1) (Fig. 1A) was used to identify a 130 kb bacterial artificial chromosome (bac) clone (PSCA probe) that in turn was used in the FISH analysis in accordance with the manufacturer's protocol (Genome Systems Inc.) The bac clone so identified and used in the FISH analysis was BACH-265B12 (Genome Systems, Inc. control number 17424). *

Please replace the paragraph beginning at page 104, line 19 with the following rewritten paragraph.

C34 * The lower panel of Figure 47 shows an ethidium bromide-stained agarose gel of RT-PCR analysis of murine PSCA transcript expression patterns in various mouse tissues. The RT-PCR was prepared using Ultraspec.RNA (Biotex), and cDNA cycle kit (Invitrogen). Primers corresponding to a region within exon 1 and exon 3 of PSCA were used to amplify a 320 bp fragment. The exon 1 primer sequence is as follows:

5' primer: 5'-TTCTCCTGCTGGCCACCTAC-3' (SEQ ID NO:8). The exon 3 primer sequence is as follows:

C34
3' primer: 5'-GCAGCTCATCCCTTCACAAT-3' (SEQ ID NO:9). As a control, to demonstrate the integrity of the RNA samples isolated from the various mouse tissues, a 300 bp G3PD fragment was amplified. --

Please replace the paragraph beginning at page 106, line 18 with the following rewritten paragraph.

C35
-- Murine monoclonal antibodies were raised against a GST-PSCA fusion protein comprising PSCA amino acid residues 18-98 of the PSCA amino acid sequence (SEQ ID NO:2) (FIG. 1B) and expressed in E. coli, utilizing standard monoclonal antibody production methods. The following seven anti-PSCA monoclonal antibodies, produced by the corresponding hybridoma cell lines deposited with the American Type Culture Collection on December 11, 1998, were utilized in this study: --

Please replace the paragraph beginning at page 118, line 28 with the following rewritten paragraph.

C36
* First strand cDNA was synthesized from hybridoma RNA using a primer from the constant region of the heavy chain (CH3'). The variable region was amplified using CH3' and a primer designed to the leader sequence (HLEAD.1 and HLEAD.2). The resulting PCR product is sequenced and the complementarity determining regions (CDRs) are determined using the Kabat rules. The nucleotide (SEQ ID NOS:10, 12, and 14) and amino acid (SEQ ID NOS:11, 13, and 15) sequences are shown in FIGS. 58, 59 and 60, respectively. An amino acid alignment of the CDRs of these three Mabs is shown in FIG. 61. --